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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,918	03/27/2001	Arthur M. Krieg	C1039/7048 (AWS)	4953

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	10

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

F 10

Office Action Summary

Application No.	Applicant(s)
09/818,918	Krieg et al
Examiner	**Art Unit**
Jane Zara	1635

-- ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 26, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-18* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Mar 27, 2001* is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Office action is in response to the communication filed December 26, 2002, Paper No. 9.

Claims 1-18 are pending in the instant application.

Election/Restriction

Applicant's election with traverse of SEQ ID Nos: 39, 43-45 in Paper No.9 is acknowledged. The traversal is on the ground(s) that the restricted nucleic acid sequences comprise a related class of chemical compounds having a generic common structural entity and should therefore not be restricted as separate molecules. This is not found persuasive because each nucleic acid sequence requires a separate search and is considered a distinct molecule, despite the fact that it shares a common dinucleotide motif (CpG). The search of all of the sequences claimed would pose an undue burden on the searching facilities and on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

SEQ ID Nos: 37, 38, 40, 42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No 9.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification and claims do not describe elements which are essential to the genus comprising atopic conditions. Furthermore, the specification and claims do not indicate what distinguishing attributes are concisely shared by the members of the genera comprising nucleic acids depicted by the generic formulae X_1CGX_2 or $X_1X_2CGX_3X_4$. The scope of the claims includes numerous structural variants, and each of these genera is highly variant because a significant number of structural differences between genus members is permitted for the genera comprising nucleic acids depicted by the formulae X_1CGX_2 or $X_1X_2CGX_3X_4$. Concise structural features that could distinguish compounds in the genera comprising atopic conditions, or comprising nucleic acids of the generic formulae X_1CGX_2 or $X_1X_2CGX_3X_4$, are missing from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, no general guidance is what is needed for these broad genera. Since the disclosure fails to describe the common attributes or characteristics concisely identifying members of the proposed genera, and because each genus is highly variant, the description provided is insufficient. One of skill in the art would reasonably conclude that the disclosure fails

to provide a representative number of species to describe the various genera claimed. Thus, Applicant was not in possession of the claimed genus.

Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of modulating the immune response in mice and treating asthma in mice comprising the administration of CpG containing oligonucleotides comprising SEQ ID No: 10, does not reasonably provide enablement for the ability to treat any and/or all atopic conditions in any organism comprising the administration of any CpG containing oligonucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The claims are drawn to compositions and methods for treating any atopic condition in an organism comprising the administration, by any route, of an immunostimulatory nucleic acid comprising the formula X_1CGX_2 .

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention over the scope claimed.

The state of the prior art and the predictability or unpredictability of the art. CpG containing oligonucleotides are currently being investigated for exerting their immunotherapeutic effects in various organisms (See Krieg et al, Weiner and McCluskie et al for recent advances using CpG oligonucleotides). Biological responses to the administration of CpG containing oligonucleotides vary, however, depending on the mode of administration and the organism (See

McCluskie et al in its entirety, and especially on page 296; Also see Krieg et al on page 524). Weiner states furthermore that the molecular mechanisms of CpG oligonucleotides' immunostimulatory effects are not yet understood (See especially page 461). And while the biological effects of some chemical modifications have been studied for CpG containing oligonucleotides, such as 2'-O-methyl modifications, phosphorothioate internucleotide linkages and 5-methyl cytosine substitutions, the incorporation and positioning of chemical modifications relative to the CpG dinucleotide are highly unpredictable (See Agrawal et al especially on pages 78-80; See also pages 31-32 of the instant specification).

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of treating any and/or all atopic conditions comprising the administration of any immunostimulatory nucleic acid comprising the formula X_1CGX_2 . The specification teaches an increase in immunomodulation in mice (and comprising conversion from a Th2 to a Th1 immune response), and treatment of asthma in a mouse model comprising the administration of SEQ ID NO: 10. One skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of the successful treatment of any and/or all atopic conditions in any organism comprising the administration by any route of any immunostimulatory nucleic acid comprising the formula X_1CGX_2 in view of the lack of guidance in the specification and known unpredictability associated with the ability to predict the biological effects exerted by CpG containing oligonucleotides in any and/or all organisms and

further comprising treatment effects provided for any and/or all atopic conditions in any organism. The specification as filed fails to provide particular guidance which resolves the known unpredictability in the art associated with effects provided in vivo in any and/or all organisms upon administration via any route of CpG containing oligonucleotides, and further whereby treatment effects are provided in any and/or all organism for any and/or all atopic conditions.

The breadth of the claims and the quantity of experimentation required. The breadth of the claims is very broad. The claims are drawn to compositions and methods for treating any atopic condition in an organism comprising the administration, by any route, of an immunostimulatory nucleic acid comprising the formula X_1CGX_2 . The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of accessible target sites, modes of delivery and formulations to target appropriate cells and /or tissues in any and/or all organisms, and further whereby treatment effects are provided for any and/or all atopic conditions. Since the specification fails to provide particular guidance for the treatment of any and/or all atopic conditions comprising administration by any route of any CpG containing oligonucleotide, and since determination of these factors for a particular CpG containing oligonucleotide and for a particular atopic condition, route of administration and organism is highly unpredictable, it would require undue experimentation to practice the invention over the broad scope claimed.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ram R. Shukla

RAM R. SHUKLA, PH.D
PATENT EXAMINER

JZ

March 6, 2003